Paper 19

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte FABRIZIO SAMARITANI and PATRIZIA NATALE

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Appeal 2001-1738
Application 08/913,748[1]

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Before: WILLIAM F. SMITH, Administrative Patent Judge, and McKELVEY, Senior Administrative Patent Judge, and MOORE, Administrative Patent Judge.

McKELVEY, Senior Administrative Patent Judge.

Decision on appeal under 35 U.S.C. § 134

The appeal is from a decision of a primary examiner rejecting claims 1-16. We affirm, but designate our affirmance as a new ground of rejection under 37 CFR § 1.196(b).

A. Findings of fact

The record supports the following findings by at least a preponderance of the evidence.[2]

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[1] Application for patent filed 21 November 1997. Applicants claim priority based on PCT application PCT/EP95/01055, filed 21 March 1995. The real party in interest is Applied Research Systems ARS Holding N.V. (Appeal Brief, page 1).

[2] To the extent these findings of fact discuss legal issues, they may be treated as conclusions of law.

The claims

1. The claims on appeal are claims 1-16.

2. According to applicants, the claims stand or fall together. We therefore decide the appeal on the basis of claim 1. 37 CFR § 1.192(c)(7).

3. Claim 1, the only independent claim in the application, reads:

> A stable, liquid pharmaceutical composition comprising recombinant human Chorionic Gonadotropin and a stabilizing amount of mannitol.

The rejection

4. Claims 1-16 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over PCT international application WO 93/11788, published 24 June 1993 (**PCT application**).[3]

Applicants' invention

5. The invention relates to a liquid formulation containing human Chorionic Gonadotropin (hCG) stabilized with mannitol.

6. According to applicants, it is known that highly purified proteins easily undergo degradation due to contact with atmospheric agents (specification, page 1, lines 7-8).

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[3] The PCT application is prior art under 35 U.S.C. § 102(b).

7. Further according to applicants, degradation is more evident for proteins produced by recombinant DNA techniques (specification, page 1, lines 8-9).

8. Still further according to applicants, the proteins are usually stabilized with saccharides, such as lactose, or with mannitol, or with other proteins or aminoacids (specification, page 1, lines 10-12).

9. An hCG composition is administered as a pharmaceutical in the form of an injectable formulation. The specification (page 1, lines 13-16) tells us:

> The injectable stabilised formulations of gonadotropins are obtained with a process which includes always a step of lyophilisation to obtain a dry powder; in such a way the stabilised formulations are able to maintain a longer cycle life, even if stored at room temperature.

10. Applicants acknowledge the PCT application as prior art in their specification (specification, page 1, line 17). Specifically, applicants note (specification, page 1, lines 17-21):

> WO 93/11788 [the PCT application] describes lyophilised gonadotropin-containing pharmaceutical compositions stabilised with sucrose, alone or in combination with other stabilising agents. In said patent application it is shown that the stability provided to the lyophilised compositions under study by sucrose was better than that provided by lactose or mannitol.

11. Applicants allege (specification, page 1, lines 22-25):

> No liquid stabilised formulations of gonadotropins have been described until now. It is highly desirable to obtain such liquid formulations so as to have the compositions ready to be injected and to avoid the reconstitution of lyophilised powder, thus simplifying the way of use.

12. Our reading of the specification reveals that applicants believe that they have found that a liquid formulation of recombinant hCG [also referred to as rec-hCG or r-hCG] stabilized with mannitol (1) has a decent shelf-life and (2) can be directly used as a liquid in injectable form without the need to reconstitute a lyophilized powder.

13. The preparation of a liquid formulation of rec-hCG and mannitol is described (specification, page 5, lines 17-29).

14. In their Appeal Brief (Paper 15, page 3), applicants call attention to Tables 10, 11, 12, 13, 14 and 15 as evidence of the patentability of their claimed invention. Data in the Tables is apparently based on experimental work.[4]

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[4] Applicants rely on experimental data set out in the specification in support of the appeal. We likewise have relied on the data and found it material in rendering our decision. Moreover, in reaching our decision, we have made the following assumptions: (1) the data set out in the specification upon which applicants rely is based on actual experimentation, (2) the data is accurately set out in the specification and (3) the data is not based on prophetic examples [see Hoffmann-La Roche, Inc. v. Promega Corp., 1999 U.S. Dist. LEXIS 19059, Civil Action C-93-1748-VRW (N.D. Cal. Dec. 7, 1999) (Findings of Fact 56-60, 63-66, 69, 105-106, 112, 131 and 136 and Conclusions of Law 32 and 35)]. We also have relied on the fact that there is no other data known to applicants or the real party in interest which (1) would tend to contradict the experimental data set out in the specification and (2) was not called to our attention in the brief and/or reply brief on appeal [see 37 CFR § 1.56(b)(2)]. If any of our assumptions are not correct, applicants should immediately notify the board in the form of a request for reconsideration.

15. To understand Tables 10-15, one must first appreciate Table 7, which describes four (4) compositions, which we designate as 1 through 4:

1. r-hCG/5000/S01 contains 10000 units r-hCG and 102.6 units sucrose
2. r-hCG/5000/M01 contains 10000 units r-hCG and 54.6 units mannitol
3. r-hCG/10000/S01 contains 20000 units r-hCG and 102.6 units sucrose
4. r-hCG/10000/M01 contains 20000 units r-hCG and 54.6 units mannitol[5]

16. One immediately notes that the ratio of sucrose to r-hCG is slightly less than twice the ratio of mannitol to r-hCG [102.6/10000 = 0.0.01026 whereas 54.6/10000 = 0.00546 for Compositions 1 and 2, respectively, and 102.6/20000 = 0.00513 and 54.6/20000 = 0.00273 for Compositions 3 and 4, respectively].

17. According to the specification, Tables 10 and 11 report the purity determined by HPSEC[6] for 5,000 and 10,000 IU strength respectively. The data is said to show that even after three weeks at 50°C, the purity is higher in the formulations containing mannitol compared to the formulations containing sucrose (specification, page 4, lines 13-16).

In Table 7, the formulation is identified as "r-hCG/1000/M01" (emphasis added). Based on other Tables we discuss, infra, we suspect the 1000 is a typographical error and that applicants meant 10000. Accordingly, we use 10000 and not 1000.

We are told in the specification that purity was measured by HPSEC analyses using standard conditions set out in the specification. However, there is no testimony, for example, in the form of a Rule 132 declaration, which explains (a) the reason why the test is being used and why the data is being relied upon; (b) how the test is performed; (c) how the data is generated using the test; (d) how the data is used to determine a value; (e) the acknowledged accuracy of the test; and (f) any other information which would aid the USPTO, including the board, in understanding the significance of the test or data. Hence, on this record, we do not know what weight, if any, should be assigned to HPSEC tests and data generated therefrom.

18. The data reported in Table 10 seems to show that the "purity" in terms of a percentage (Time = 0 weeks being 100%) of Compositions 1 and 2 is essentially the same after 1 and 3 weeks at 50°C and after 3 weeks at 40°C (specification, page 17, Table 10) (higher percentage set out in bold):

	50°C		40°C
	1 week	3 weeks	3 weeks
r-hCG/5000/SO1	**90.0**	86.3	97.2
r-hCG/5000/MO1	89.5	**88.3**	**97.6**

19. The data reported in Table 11 seems to show that the "purity" in terms of a percentage (Time = 0 weeks being 100%) of Compositions 3 and 4 are somewhat better for mannitol vis-a-vis sucrose in terms of a shelf-life at 50°C, but shelf-life is slightly better for sucrose vis-a-vis mannitol in terms of a shelf-life at 40°C. (specification, page 17, Table 11) (higher percentage set out in bold):

	50°C		40°C
	1 week	3 weeks	3 weeks
r-hCG/10000/SO1	91.8	88.9	**97.9**
r-hCG/10000/MO1	**93.4**	**92.1**	97.2

20. Tables 12 and 13 are said to report the purity of the α-subunit of r-hCG determined by "reverse phase HPLC"[7]

[7] Our comments with respect to HPSEC, n.6, supra, also apply to "reverse phase HPLC".

after 1 week storage at 50°C for sucrose and mannitol formulations (specification, page 4, lines 16-18). The data is said to "confirm the better stability of the formulation containing mannitol in comparison to that containing sucrose" (specification, page 4, lines 18-20).

21. The α-subunit percentage for Compositions 1 through 4 after 1 week at 50°C (α-subunit % = 100 at time = 0 weeks) is said to be the following:

1.	r-hCG/5000/SO1 (sucrose)	90.2
2.	r-hCG/5000/MO1 (mannitol)	94.7
	and	
3.	r-hCG/10000/SO1 (sucrose)	92.4
4.	r-hCG/10000/MO1 (mannitol)	95.1

22. According to the specification (page 5, lines 1-3), Tables 14 and 15 report bioactivity assay[8] with no appreciable bioactivity decrease being observed after 24 weeks at 4°C and 25°C in compositions with mannitol.

23. It is true that Tables 14 and 15 report data at the 24 week time period for mannitol. No data is reported for sucrose. Accordingly to the extent the data in Tables 14 and 15 are replied upon to compare r-hCG's stabilized with mannitol vis-a-vis those stabilized with sucrose, the data are not convincing.

24. Further according to counsel, Table 14 shows that when evaluated by bioassay of the International Unit content, the

[8] Our comments with respect to HPSEC, n.6, supra, also apply to "bioassay" tests and data reported from those tests.

mannitol-containing liquid formulation lost 27% of its IU/ml after three weeks at 50°C while the sucrose stabilized liquid formulation lost 36% over the same time period at the same temperature (Appeal Brief, page 3).

25. We are unsure as to how counsel arrived at the 27% and 36% figures for the data in the three week column of Table 14. As best we can tell, the percentages should be 26.5% for sucrose and 18.4 for mannitol:

Sucrose (9194 - 6757)/9194 = 0.265 = 26.5%

Mannitol (8548 - 6977)/8548 = 0.184 = 18.4%

We assume that applicants would maintain that the lower the percentage, the better the result. However, as we have noted earlier, we are unable, on this record, to make a finding as to whether the results are due to (1) sucrose v. mannitol or (2) the amount of sucrose v. the amount of mannitol or (3) both. Moreover, we note that after a 3-week period the IU/ml for sucrose (6757) is not all that different than the IU/ml for mannitol (6977).

26. Still further according to counsel, Table 15 shows that the mannitol liquid formulation lost 24% measured in IU/ml after 6 weeks at 40°C whereas the sucrose liquid formulation lost 32.5% over the same time period at the same temperature (Appeal Brief, page 3).

27. We have no idea where the 24% and 32.5% figures come from. As best we can tell, if one starts with T = 0, then the percentages should be:

Sucrose (20273 - 14977)/20273 = 0.261 = 26.1%

Mannitol (18919 - 14680)/18919 = 0.224 = 22.4%.[9]

28. Counsel argues that the results of Tables 10-15 "are surprising and unexpected." Why? In terms of the data in Table 10 and 11, we have not been told whether a 3-week period is practical shelf-life or whether r-hCG compositions are normally stored at 40°C or 50°C. In other words: "From a practical point of view, what would one skilled in the art understand to be the normal shelf-life needed for liquid r-hCG compositions?" Additionally, we are in no position to determine, on this record, that any differences in results are not due to the difference in the ratio of r-hCG to sucrose v. the ratio of r-hCG to mannitol. The data in Tables 14 and 15 at the 3-week and 6-week periods shows the IU/ml figures to be similar (6757 v. 6977 and 14977 v. 14680). We have not been told whether a person having ordinary skill in the art would view these differences to have any practical significance.

29. We decline to find that the data in Tables 7 and 10-15 establish any superior, surprising or unexpected result for mannitol v. sucrose.

The prior art--PCT application

30. According to the PCT application (page 1, lines 8-11):

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[9] Arguably, one might obtain counsel's percentages if the "base" is T = 4 weeks.

It is known that highly purified proteins are time-unstable and are stabilized, for instance, in admixture with saccharides, such as lactose and mannitol ***.

31. Further according to the PCT application (page 2, lines 31-33):

Gonadotropins which are found on the market are stabilized by means of saccahrides, for instance hCG is stabilized by means of mannitol (Profasi®, SERONO) ***.

32. Still further according to the PCT application (page 3, lines 3-6):

We have now found that sucrose confers a better stability to the formulation of gonadotropins and in particular to the form of these glycoproteins which have been prepared with the recombinant DNA technique.

33. An object of the invention described by the PCT application (page 3, lines 12-22):

is to provide a process for the preparation of *** [a] pharmaceutical composition, the step of lyophilising an aqueous solution of the components. Another object is to provide a presentation's form of *** [the] pharmaceutical composition comprising the said solid mixture hermetically closed in a sterile condition within a container suitable for storage before use and suitable for reconstitution of the mixture for injectable substances.

Another object is to provide a solution for said solid mixture reconstituted into an injectable solution.

34. The PCT applications says that "biological tests have been performed" (page 4, line 6) and that the results of those tests (page 4, lines 12-15):

> show that the most stable formulations among those tested are those containing sucrose, i.e., formulations with sucrose alone and with sucrose plus glycin.

35. One study is described as follows (page 19, lines 5-16):

> A study has been also performed on urinary hCG formulations by using sucrose (formulation "a", 30 mg sucrose), lactose (formulation "b", 10 mg lactose) or mannitol (formulation "c", 20 mg mannitol) as stabilizers in 3 ml vials containing 500 I.U./vial hCG.
>
> Tab. 10 gives the estimated values derived by the biological assay performed at different times for said hCG formulations stored at a temperature of 55°C.
>
> Once again, sucrose is shown to be the most suited excipient in order to preserve hCG stability ***.

36. Part of a table at Tab. 10 reveals the following (page 20), where 3W means 3 weeks and 6W means 6 weeks:[10]

Composition	T = 0	3W	6W
a	511	567	597
b	534	355	428
c	449	332	244

[10] We note that the ratio of hCG to sucrose is not the same as the ratio of hCG to mannitol. Hence, we find it difficult to assess the weight to be given the data set out in Tab. 10. See also Finding 25.

European Patent Application 0 448 146 A1

37. The PCT application mentions European Patent Application 0 448 146 A1, published 25 September 1991 (**EPO**).

38. EPO describes the "State of the Art" partially as follows (page 2, lines 10-24):

> Relatively pure gonadotropin preparations are commercially available. For example, compositions containing naturally derived human menopausal gonadotropin ("HMG") and naturally derived human chorionic gonadotropin ("HCG") are available as freeze-dried preparations under the trade designations "Humegon" and "Pregnyl," respectively, from Organon International, bv of Oss, NL. Pregnant mare gonadotropin is also available in freeze dried form from the same company.
>
> A bulking agent, e.g., mannitol, is added to these preparation before lyophilization. They do not require the addition of a stabilizer to ensure an adequate shelf-life. Evidently whatever natural contaminants remain after the purification process act to stabilize the preparations in freeze-dried form.
>
> Recently however, with the advent of more effective production and purification techniques, preparations of certain very pure gonadotropins are insufficiently stable. They degrade in a relatively short time, losing activity. In order to prevent or slow down this degradation, attempts were made to freeze-dry (lyophilize) the preparations. Lyophilization has only been partially successful however.
>
> A need exists for a gonadotropin containing pharmaceutical preparation which is stable over a sufficient long period of time for the product to be manufactured, shipped, and stored prior to use. The need is especially

great for a stable preparation containing more than one gonadotropin.

B. Discussion

1. Scope of claim 1

a.

We begin our analysis by construing the scope of applicants' claim 1. As noted above, claim 1 reads:

> A stable, liquid pharmaceutical composition comprising recombinant human Chorionic Gonadotropin and a stabilizing amount of mannitol.

The composition must:

(1) be in "liquid" as opposed to "solid" form;

(2) be capable of being used as a pharmaceutical;

(3) contain hCG in "recombinant" as opposed to a natural form; and

(4) contain a "stabilizing" amount of mannitol.

The so-called "preamble" states that the composition is "stable".

b.

Our appellate reviewing court has provided guidance with respect to the weight to be given words in a preamble. Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc., 246 F.3d 1368, 1373, 58 USPQ2d 1508, 1513 (Fed. Cir. 2001) (if the body of the claim sets out the complete invention, and the preamble is not necessary to give "life, meaning and vitality" to the claim,

"then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation"); Rowe v. Dror, 112 F.3d 473, 478, 42 USPQ2d 1550, 1553 (Fed. Cir. 1997) ("A claim preamble has the import that the claim as a whole suggests for it. Where a patentee uses the claim preamble to recite structural limitations of his claimed invention, the PTO and courts give effect to that usage. Conversely, where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention, the preamble is not a claim limitation." (citations omitted)).

Federal Circuit precedent also provided guidance with respect to the construction of claims undergoing examination. Burlington Industries v. Quigg, 822 F.2d 1581, 1583, 3 USPQ2d 1436, 1438 (Fed. Cir. 1987) (claims undergoing examination are given their broadest reasonable construction consistent with the specification); In re Prater, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969) (same).

c.

In this case, we have found no definition of the term "stable" in the specification. The specification tells us that "[t]he main object" of applicants' invention is a pharmaceutical composition containing hCG "stabilised" with a sugar, preferably mannitol (page 1, lines 28-32). Although data in the specification reports results after as long as a 24-week period

(page 20), nothing in the specification would support a definition of "stable" in the claims as requiring stability for a 24-week period or any other particular period.

We also note that the claim otherwise requires a "stabilizing" amount of mannitol. Various tests are described in which varying amounts of mannitol are mixed with r-hCG. Use of the amounts of mannitol set out in the specification presumably would result in a "stable" composition. Hence, it can be argued that "stable" adds nothing to the claim which is not already there by virtue of the limitation requiring a stabilizing amount of mannitol. Accordingly, we decline to give any weight to the word "stable" in the preamble of claim 1. However, even if we did give the term some weight, in light of the fact that applicants' claim 1 is to be construed broadly consistent with the specification, we would hold that "stable" at best would mean that the composition is stable for any period of time.

Nothing in claim 1 requires that the liquid pharmaceutical composition be in liquid form for any particular time. Hence, the claim reads on lyophilized r-hCG/mannitol compositions which have been reconstituted to liquid form just prior to administration.

2. Prima facie obviousness

An understanding of our rationale in support of obviousness requires, inter alia, (1) an understanding of the broad scope of claim 1, (2) practices said to be used in the prior art and

(3) the extent to which claim 1 would preclude similar practices which we hold to have been obvious over the practice which is explicitly described in the prior art.

a.

It appears from the prior art that once upon a time the "art" used natural hCG as the primary source for pharmaceutical application. Apparently, natural hCG is quite stable, at least if we are to believe EPO. According to EPO, some natural hCG products do not need stabilizers, although we note that a "bulking agent" amount of mannitol (now understood to be a stabilizer) is said to have been added to hCG prior to lyophilization. Natural contaminants are said to be a possibility for explaining why natural hCG remained stable after lyophilization. EPO reveals, however, that as more pure hCG came to be, stabilization problems developed.

Somewhere along the line hCG in recombinant form [r-hCG] came to exist--all would recognize that r-hCG would be quite pure. Hence, given its purity, it reasonably would have been expected from EPO that r-hCG would need a stabilizer. The PCT application confirms what one skilled in the art would have divined from EPO. According to the PCT application, sucrose is "the solution" to stability problems.

To be sure, the PCT application at first blush would appear to be a basis for one skilled in the art to tout sucrose in favor of mannitol, saying that (1) the "most stable formulations"

(page 4, line 12) are those with sucrose and (2) sucrose "is much better than mannitol" (page 19, line 15). The PCT application nevertheless reveals that mannitol-stabilized hCG has been commercially marketed under the mark Profasi®. If a pharmaceutical product has been marketed, as applicants' assignee seems to say it was in the PCT application and their Reply Brief, then mannitol stabilized hCG cannot be considered a technical curiosity. Generally, companies do not market products which do not work.

The record does not show the precise nature of the Profasi® product. However, counsel for applicants favors us with the following discussion in the Reply Brief (page 2):

> *** the commercial product which has been referenced (Profasi) is a product of a company related to the real party in interest herein and is urinary hCG and not recombinant hCG as claimed.

While a statement of counsel cannot take the place of evidence in the record, we accept counsel's representation for the purpose of deciding the appeal.

b.

We find that the difference between

(1) the "commercial product" (Profasi®) and other hCG compositions described on pages 19-20 of the PCT application and

(2) the subject matter of claim 1

is that claim 1 requires r-hCG with mannitol whereas the prior art describes natural hCG with mannitol.

The PCT application, however, makes it more than clear that r-hCG is a viable alternative to natural hCG. The PCT application describes efforts to find a solution to stabilization problems associated with hCG, in general, and r-hCG in particular (page 3, lines 3-6). We hold that one skilled in the art would have found it obvious to use r-hCG in place of natural hCG to make the compositions described by the PCT application. The use of purified r-hCG in place of natural hCG is nothing more than the use of a known product for its known use to achieve an expected result, i.e., a pharmaceutical composition with a known use. Cf. In re Gorman, 933 F.2d 982, 987, 18 USPQ2d 1885, 1889 (Fed. Cir. 1991) (the claim elements appear in the prior art in the same configurations, serving the same functions, to achieve the results suggested in the prior art).

Once one accepts the fact that one skilled in the art would have found it obvious to use r-hCG in place of natural hCG to make a lyophilized product like the commercial natural hCG Profasi® product, then one also has to immediately accept the proposition that the lyophilized product with r-hCG would be used in practice by reconstituting it into an injectable solution (PCT application, page 3, lines 21-22). It is the otherwise obvious r-hCG/mannitol injectable solution which we feel renders obvious the subject matter of claim 1. Stated in other terms, we find that one using a reconstituted injectable otherwise obvious

solution of r-hCG and mannitol would infringe applicants' claim 1. For a variety of reasons, many of which are apparent from our findings, we are not prepared to say that applicants' specification evidences unexpected results. However, assuming arguendo it does, then what surfaces in this appeal that applicants' claim is too broad in the sense of 35 U.S.C. § 103. In re Muchmore, 433 F.2d 824, 826, 167 USPQ 681, 683 (CCPA 1970) (claims which include obvious subject matter and non-obvious subject matter are not patentable under § 103). A claim which would preclude the public from using an injection solution reconstituted from lyophilized r-hCG and mannitol runs afoul of § 103.

c.

Since our rationale in support of obvious is not that of the examiner, it would be fair to say that applicants have not had a reasonable opportunity to anticipate our rationale and address it. We nevertheless feel it appropriate to address some of applicants' arguments.

According to applicants (Appeal Brief, page 3), it has been established that the stability of lyophilized hCG compositions containing sucrose "is better" than similar compositions stabilized with other materials, such as lactose or mannitol. Accordingly, applicants make an argument in the form of a question to the effect: "Why in the world would one skilled in the art even 'try' to use mannitol in place of sucrose?" While

applicants' argument is superficially plausible in the face of the PCT application, it falls apart when one takes into account the fact that hCG products with mannitol have been commercially sold. Thus, even if one accepts the proposition that the data in the PCT application supports a finding that sucrose is better than mannitol, it remains the fact that those skilled in the art would have understood that commercial hCG/mannitol products perform in an acceptable manner. We believe one skilled in the art will not lightly reject commercial embodiments.

3. Applicants' data

The Federal Circuit has determined that board is given broad deference in its weighing of the evidence before it. In re Inland Steel Co., 265 F.3d 1354, 1366, 60 USPQ2d 1396, 1405-06 (Fed. Cir. 2001). Whether evidence shows unexpected results is an question of fact and party asserting unexpected results has the burden of proving that the results are unexpected. In re Geisler, 116 F.3d 1465, 1469-70, 43 USPQ2d 1362, 1364-5 (Fed. Cir. 1997). For a variety of reasons, we decline to credit much of the technical data offered by applicants in support of non-obviousness. Accordingly, we decline to find that applicants have sustained their burden of establishing unexpected results.

a.

We do not know whether Compositions 1 through 4 (see Finding 15) provide a basis for comparing hCG/sucrose v. hCG/mannitol. The amount of sucrose and mannitol in the hCG

compositions differs. See Findings 16 and 25. There is no testimony before us which explains why data based on the compositions would be accepted by those skilled in the art in the face of the different ratios.

b.

We do not know whether the data set out in Tables 10 and 11 would be accepted by a person skilled in the art as showing that use of sucrose is not as good as use of mannitol. We cannot overemphasize the fact that one relying on data to establish has a burden of establishing that unexpected results are actually obtained and the significance of those results to one having ordinary skill in the art. Cf. In re Klosak, 455 F.2d 1077, 1080, 173 USPQ 14, 16 (CCPA 1972) (inventor must show that the results claimed to obtained with a claimed invention are actually obtained with the invention).

Assuming that the different ratios of hCG to sucrose or mannitol have no practical effect on other testing described in the specification, then we note that in the case of Compositions 1 and 2, after 1 week at 50°C the stability data (90.0) for r-hCG/sucrose would appear to be higher (and therefore presumably better) than the data (89.5) for r-hCG/mannitol (see Finding 18). A similar observation can be made with respect to Compositions 3 and 4 when tested at 40°C for 3 weeks (see Finding 19). Even if we were inclined to give the term "stable" in the preamble of claim 1 some claim limiting significance, it would not exclude

an r-hCG/mannitol composition which has been stored for 1 week or 3 weeks.

c.

Tables 12 and 13 involve purity tests of the α subunit of r-hCG. But, the claims are not limited to the α subunit of r-hCG. What significant fact are we to divine from data limited to the α subunit? On this record, we are not told!

d.

The data in Tables 14 and 15 are unexplained. We recognize that there is data, but we have no idea of its significance to one of ordinary skill in the art. Applicants have not sufficiently explained the significance of the data. See also n.6, supra, and Findings 23-27.

C. Order

Upon consideration of the appeal, and for the reasons given, it is

ORDERED that the rejection of claims 1-16 is affirmed.

FURTHER ORDERED that in view of the fact that we have relied on additional prior art and new rationale, the affirmance of the rejection is a new ground of rejection under 37 CFR § 1.196(b).

FURTHER ORDERED that under 37 CFR § 1.196(b) our new ground of rejection shall not be considered final for purposes of judicial review.

FURTHER ORDERED that applicants, **WITHIN TWO MONTHS FROM THE DATE OF ENTRY OF THIS DECISION**, must exercise one of the following two options with respect to the new grounds of rejection to avoid termination of proceedings (37 CFR § 1.197(c)) as to the rejected claims:

> (1) Submit an appropriate amendment of the claims so rejected or a showing of facts relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the application will be remanded to the examiner.
>
> (2) Request that the application be reheard under § 1.197(b) by the Board of Patent Appeals and Interferences upon the same record.

FURTHER ORDERED that since the appeal was presented on the basis that all claims stand or fall together, and that we have decided the appeal on that basis, should applicants elect to proceed before the examiner on remand [Option (1), supra], then our affirmance should be construed to be without prejudice to applicants presenting argument before the examiner maintaining that any of claims 2 through 16 are separately patentable from claim 1.

FURTHER ORDERED that no time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED
(37 CFR § 1.196(b))

_____	
WILLIAM F. SMITH	
Administrative Patent Judge	
_____	
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